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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,634	12/09/2005	Leon Carlock	4981-000011/NPB	6748

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EXAMINER	
WANG, CHANG YU	
ART UNIT	**PAPER NUMBER**
1649	

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08/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,634	CARLOCK ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *61-94* is/are pending in the application.

4a) Of the above claim(s) *79-94* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *61-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *61-94* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/26/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO AMENDMENT

Status of Application/Amendments/claims

1. Applicant's amendment filed June 5, 2007 is acknowledged. Claims 1-60 are cancelled. Newly added claims 61-94 are pending in this application. Claims 79-94 are withdrawn with traverse (p.9 of the response filed on March 3, 2006) from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention because they are new and correspond to a non-elected invention as set forth in the restriction requirement of 9/19/06; there being no allowable generic or linking claim.

2. Claims 61-78 are under examination in this office action.

3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response.

4. Applicant's arguments filed on June 5, 2007 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections/Objections Withdrawn

5. The rejection of claims 1, 2, 7 and 41 under 35 U.S.C. 112, second paragraph, for being indefinite because of the recitations "fragment", "a part", "mutant", "fusion partner peptide/polypeptide with a second amino acid sequence" is moot because the claims are canceled.

The rejection of claims 1-4 and 41 under 35 U.S.C. 102(b) for being anticipated by Stoffel et al. (Hoppe-Seyler's Z. Physiol. Chem. 1982. S. 1117-1131) is moot because the claims are canceled.

Claim Rejections/Objections Maintained

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 61-63, 66-70, 73-77 and 78 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a recombinant polypeptide comprising a fragment consisting of SEQ ID NOs: 6 and 12 or aa 31-72 of SEQ ID NO:6, and a fusion protein wherein the fragment is fused to the fusion protein, does not reasonably provide enablement for a recombinant polypeptide comprising a fragment having an amino acid sequence of any part of PLP that begins with any internal amino acid residue that is encoded by the translation initiation site of an IRES in mRNA encoding SEQ ID NO:6 or aa 31-72 of SEQ ID NO:6 as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in the scope with these claims. The rejection is maintained for the reasons made of record as directed claims1-2, and 41 in the previous office action (Paper No. 20061221).

Applicant argues that new claims 61-63, 66-70, 73-77 and 78 are enabling because the claims only encompass native sequences of PLP and beginning at the start codon of the IRES and the sequences of PLP are conserved among different species (p. 20-23, 26 of the response). Applicant argues that the claimed polypeptides have biology activity in promoting myelination, neuronal viability and oligodendrocyte survival and differentiation and can be used in vivo for pharmaceutical purposes (p.21, 26-27 of the response). Applicant's arguments have been fully considered but they are not persuasive.

In contrast to Applicant's assertion on p. 20-23 and 26-7 with regard to enablement of the claimed polypeptides, the specification fails to teach that a polypeptide comprises any part of PLP that begins with any internal amino acid residue that is encoded by translation initiation site of an IRES of mRNA encoding SEQ ID NO:6 or aa 31-72 of SEQ ID NO:6 would generate a functional active fragment. Based on the prior art and specification, Applicant is enabled for a recombinant polypeptide comprising a fragment consisting of SEQ ID NOs: 6 and 12 or aa 31-72 of SEQ ID NO:6, and a fusion protein wherein the fragment is fused to the fusion protein such as GFP, His or Fv since only a polypeptide comprising the functional active domain of PLP (aa 215-232 of PLP corresponding to aa 45-62 of instant SEQ ID NO:6) has the activity of stimulating neuronal activity and meylination. However, claims 61-63, 66-70, 73-78 are not limited to the molecules as set forth above but also encompass fragments that begin with any internal amino acid residue of SEQ ID NO:6 or aa 31-72 of SEQ ID NO:6.

As previously made of record, the specification fails to teach that PLP fragments containing amino acid sequences other than the active domain of PLP (i.e. aa 45-62 of instant SEQ ID NO:6) would be functionally active. The specification fails to teach what specific amino acid sequences are required for the claimed polypeptides or can or cannot be changed in the claimed polypeptides and still be functionally active. Thus, a skilled artisan cannot contemplate how to make and use the claimed polypeptides that are not functionally and structurally defined and still have activity as in PLP without undue experimentation.

Accordingly, the court in *Genentech, Inc., v. Novo Nordisk*, 42 USPQ2d 1001, 1005 (1997), held that "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable", and that "reasonable detail must be provided in order to enable members of the public to understand and carry out the invention".

Thus, in that no structure and functional language is recited in the claims, the claims encompass any fragment, which the court held as not enabled. Accordingly, the rejection of claims 61-63, 66-70, 73-77 and 78 under 35 U.S.C. §112, first paragraph, as the specification does not enable the invention commensurate in scope with the claims is maintained.

7. Claims 61-63, 66-70, 73-77 and 78 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is

maintained for the reasons made of record for cancelled claims1-2, and 41 in the previous office action (Paper No. 20061221).

Applicant argues that new claims 61-63, 66-70, 73-77 and 78 meet the written description requirement because the claims only encompass native sequences of PLP and beginning at the start codon of the IRES and the sequences of PLP are conserved among different species (p. 20-23, 26 of the response). Applicant argues that the claimed polypeptides have biology activity in promoting myelination, neuronal viability and oligodendrocyte survival and differentiation and can be used in vivo for pharmaceutical purposes (p.21, 26-27 of the response). Applicant's arguments have been fully considered but they are not persuasive.

In contrast to Applicant assertion on p. 20-23 and 26-27, the specification fails to demonstrate possession of the genus of the claimed polypeptide comprising any part of PLP that begins with any internal amino acid residue that is encoded by translation initiation site of an IRES of mRNA encoding SEQ ID NO:6 or aa 31-72 of SEQ ID NO:6 would generate a functional active fragment. Based on the prior art and specification, Applicant is in possession of a recombinant polypeptide comprising a fragment consisting of SEQ ID NOs: 6 and 12 or aa 31-72 of SEQ ID NO:6 and a fusion protein wherein the fragment is fused to the fusion protein such as GFP, His or Fv that have the activity of stimulating neuronal activity and meylination. However, claims 61-63, 66-70, 73-78 are not limited to the molecules as set forth above but also encompass polypeptides comprising any part of PLP having the fragments that begin with any internal amino acid residue of SEQ ID NO:6 or aa 31-72 of SEQ ID NO:6. The

specification fails to demonstrate that Applicant is possession of such broadly claimed genus of polypeptides that have functional activity as PLP. The specification only teaches that only a polypeptide comprising the functional active domain of PLP (aa 215-232 of PLP corresponding to aa 45-62 of instant SEQ ID NO:6) has the activity of stimulating neuronal activity and meylination. However, the claims are not limited to polypeptides encompassing this functional domain of PLP but also include fragments with no structurally or functional defined sequences. The specification fails to describe what specific amino acid sequences are required and can/cannot be changed in order to maintained the activity of SEQ ID NO:6. Since the structure and function of the claimed polypeptides are not defined, a skilled artisan cannot envision the structural and functional relationship of the claimed genus and the claimed invention.

Accordingly, the court held in *Univ. California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997) that:

"One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is".

and that:

"A description of a genus of cDNAs [products] may be achieved by means of a recitation of a representative number of cDNAs [products], *defined by nucleotide sequence*, failing in the scope of the genus or of a recitation of structural features common to the members of the genus, *which features constitute a substantial portion of the genus* [emphasis added]. This is analogous to enablement of a genus under 112, [first paragraph], by showing the enablement of a representative number of species within the genus. See *In re* Angstadt, 537 F.2d at 502-03, 190 USPQ at 218".

Therefore, the rejection of claims 61-63, 66-70, 73-77 and 78 under 35 U.S.C.§ 112, first paragraph, for failing to meet the written description requirement is maintained.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 61-67, 69-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stoffel et al. (Hoppe-Seyler's Z. Physiol. Chem. 1982. S. 1117-1131 in view of Metz et al. (Somatic Cell and Mol. Genet. 1998. 24: 53-69) Cha et al. (Biotech. and Bioeng. 2000. 67: 555-574) and Pryor et al. (Protein Exp. And Purif. 1997. 10: 309-319). The rejection is maintained for the reasons made of record as applied to claims 1-4, 7, 8 and 41 in the previous office action (Paper No. 20061221).

Applicant argues that none of the applied references teach the claimed polypeptides because the PLP polypeptide disclosed in Stoffel et al. is different from the

amino acid sequence of human PIRP-M (i.e. Leu50Val of the instant SEQ ID NO:6) (p. 28 of the response). Applicant argues that the polypeptide of Stoffel et al. is an expressed peptide rather than a part of the whole protein and the polypeptide of Stoffel et al. does not show a biological activity or utility and cites *In re Stemniski* and *in re Albrecht* in support of arguments (p. 29-30 of the response). Applicant's arguments have been fully considered but they are not persuasive.

In contrast to Applicant's assertion on p. 28 of the response that the PLP sequence of the art differs from the claimed polypeptide, the examiner asserts that the PLP sequence of bovine in Stoffel et al. is the same as human PLP, which is also supported by Applicant's sequence alignment on p. 23 of the response (see No. (11) of the response). In addition, the recitation of "the fragment ...is encoded by translation initiation site of an internal ribosome entry site (IRES).... of the mRNA encoding said native proteolipid protein" in claim 1 is considered as a limitation of product-by-process, which appears to be the same as, or an obvious variant of a product of the prior art, because the different process (i.e. translation of an IRES) does not generate a structural different product.

It is noted that the courts have held that when the prior art product reasonably appears to be the same as that claimed, but differs by process in which it is produced, a rejection of this nature is eminently fair and the burden is upon the appellants to prove, by comparative evidence, a patentable difference (*In re Brown,* 173 USPQ 685 (1972)).

In addition, the IRES site in the native PLP/DM20 has existed in the molecule while the protein was identified. Further, in contrast to Applicant's assertion on p. 29-30 of the response that the PLP fragment of Stoffel et al. has no biological activity, the PLP fragment of Stoffel et al. has a biological activity as the claimed PLP fragment as

evidenced by Yamada et al. (J. Neurosci.1999. 19:2143-2151, as in IDS submitted on 6/26/07). Although Stoffel et al. do not teach the biological activity of the claimed PLP fragment, the activity of PLP and its functionally active domain are well known in the art. Yamada et al. teach that the active domain of the PLP for growth factor activity requires amino acid residues 215-232 in the PLP protein sequence (aa180-197 in the DM20; see p.2143, abstract; p. 2147, 1st col. 2nd paragraph). Since the art and instant PLP fragments are structurally identical products (i.e. the last 72 amino acids of PLP, which comprises the active domain aa 215-232 of PLP) and the activity of a molecule is determined by the structure and composition of the molecule, the PLP fragment of Stoffel et al. has the same biological activity as the claimed PLP fragment. The activity of the PLP fragment of Stoffel et al is an intrinsic or inherent property of the polypeptide of Stoffel et al. because the property of the polypeptide has already existed in the polypeptide while the polypeptide was identified. Moreover, since the structure and composition of the Stoffel's polypeptide are the same as the claimed fragment and Applicant is claiming a product rather than a method, the polypeptide of Stoffel et al. meets the limitation of the claimed PLP fragment.

"The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342,1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). " See MPEP § 2112.01 [R-3].

Although Stoffel et al. do not teach recombinant proteins containing the claimed PLP fragment and a fusion partner and also fails to teach the fusion partner as GFP,

His-tag or Fv as recited in the claims, as previously made of record, Metz et al., Cha et al. and Pryor et al. teach use of GFP or His or His-GFP to make fusion proteins containing a protein of interest and a GFP or His-tag, and teach a cleavage site between the protein of interest and the fusion partner for monitoring proteins and for protein isolation. The results from a recombinant polypeptide comprising the Stoffel's PLP fragment and a heterologous polypeptide such as His-tag or GFP are predictable because the recombinant polypeptide has the same activity as the Stoffel's PLP fragment. Use of GFP, His-GFP or His-tag for purposes of protein isolation and protein trafficking is well known in the art as taught by Metz et al., Cha et al. and Pryor et al.. The claimed PLP fragment (SEQ ID NO:6 or aa 31-72 of SEQ ID NO:6) is taught by Stoffel et al. and the activity of the Stoffel's PLP fragment is also well known in the art. It would have been obvious to one of ordinary skill in the art to generate a recombinant polypeptide comprising the PLP fragment of Stoffel et al. and a heterologous polypeptide such as GFP, His-GFP or His-tag to isolate the PLP fragment of Stoffel et al. since the activity of the recombinant polypeptide is predictably same as in the PLP fragment of Stoffel et al.. In addition, it would be also obvious to one of ordinary skill in the art to isolate the PLP polypeptide of Stoffel et al. by making a recombinant polypeptide comprising the polypeptide and a heterologous protein such as a His-tag or GFP and a cleavage site because a heterologous polypeptide such as GFP, His-GFP or His-tag has been used as a tool to purify the polypeptide of interest using a His- or GFP-affinity column and further to purify the polypeptide of interest by cleaving the recombinant polypeptide between the polypeptide of interest and the heterologous

peptide (GFP or His-tag) at the cleavage site to release the polypeptide of interest. It would be also obvious to one of skill in the art to make a recombinant polypeptide comprising the PLP fragment of Stoffel et al. and a heterologous polypeptide such as GFP, His-GFP or His-tag to monitor the trafficking of the PLP polypeptide of Stoffel et al. by detecting or monitoring His-tag or GFP proteins that are fused to the Stoffel's PLP fragment (which is the claimed PLP fragment, SEQ ID NO:6 or aa 31-72 of SEQ ID NO: 6) by fluorescent signals of GFP or antibodies against these heterologous molecules Thus, the claimed recombinant polypeptide comprising the claimed PLP fragment (SEQ ID NO:6 or aa 31-72 of SEQ ID NO:6) and a heterologous polypeptide (GFP or His-tag) is obvious over the combined teachings of applied references. One of ordinary skill in the art would have expected success in generation of a recombinant fusion protein containing the claimed PLP fragment (SEQ ID NO:6 or aa 31-72 of SEQ ID NO:2) and a fusion partner such as GFP or His6-tag because GFP and His6 have been successfully used to make fusion proteins for the purposes of monitoring and isolating interested proteins. Accordingly, the rejection of 61-67, 69-78 under 35 U.S.C. 103(a) for being unpatentable over Stoffel et al. in view of Metz et al., Cha et al. and Pryor et al. is maintained

New Grounds of Rejection

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 61-66, 72-73, and 78 are rejected under 35 U.S.C. 102(b) as being anticipated by Suteliffe (U. S. Patent No. 5,242798 issued on Sep 7, 1993 as in IDS submitted 6/26/07).

Suteliffe (U. S. Patent No. 5,242798) (Suteliffe (US'798) teaches SEQ ID NO:19, which contains a fragment having the amino acid sequence with 100% identity to the instant SEQ ID NO:6 (see sequence alignment below). Suteliffe (US'798) also teach a recombinant polypeptide comprising a fragment containing a part of a native protelolipid protein (PLP) and a fusion partner because Suteliffe (US'798) teaches fusion proteins of SEQ ID NO:19 (instant SEQ ID NO:6) (as in claims 61-66, 71-74, 76, and 78; see col.7, lines 47-69). A native PLP consists of either aa 1-276 (PLP) or aa 1-240 (DM20). The amino acid sequence of the Instant SEQ ID NO:6 corresponds to aa 205-276 of PLP or aa 170-241 of DM20 and the amino acid sequence of aa 30-72 of SEQ ID NO:6 corresponds to aa 234-276 of PLP or aa 199-241 of DM20. Since the SEQ ID NO:19 of Suteliffe (US'798) (identical to SEQ ID NO:6) is a part of PLP (i.e corresponding to aa 205-276 of PLP or aa 170-241 of DM20), the teachings of fusion proteins in Suteliffe (US'798) meet the limitations as recited in claims 61-66, 72, 73 and 78. Therefore, claims 61-66, 72, 73 and 78 are anticipated by Suteliffe (U. S. Patent No. 5,242798). The sequence search results disclose as follows:

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5242798-7
;Patent No. 5242798
;    APPLICANT: SUTCLIFFE, J. GERGOR
;    TITLE OF INVENTION: SYNTHETIC POLYPEPTIDES CORRESPONDING
;TO PORTIONS OF PROTEINOIDS TRANSLATED FROM BRAIN-SPECIFIC MRNAS,
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;RECEPTORS, METHODS AND DIAGNOSTICS USING THE SAME
;     NUMBER OF SEQUENCES: 19
;     CURRENT APPLICATION DATA:
;       APPLICATION NUMBER:  US/07/476,961
;       FILING DATE: 07-FEB-1990
;     PRIOR APPLICATION DATA:
;       APPLICATION NUMBER: 58,620
;       FILING DATE: 03-JUN-1987
;       APPLICATION NUMBER: 516,136
;       FILING DATE: 21-JUL-1983
;SEQ ID NO:7:
;       LENGTH: 121
5242798-7

  Query Match             100.0%;  Score 372;  DB 7;  Length 121;
  Best Local Similarity   100.0%;  Pred. No. 1.4e-43;
  Matches   72;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MYGVLPWNAFPGKVCGSNLLSICKTAEFQMTFHLFIAAFVGAAATLVSLLTFMIAATYNF 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         50 MYGVLPWNAFPGKVCGSNLLSICKTAEFQMTFHLFIAAFVGAAATLVSLLTFMIAATYNF 109

Qy         61 AVLKLMGRGTKF 72
              ||||||||||||
Db        110 AVLKLMGRGTKF 121
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Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 61-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Suteliffe (U. S. Patent No. 5,242798 issued on Sep 7, 1993 as in IDS submitted

6/26/07) in view of Metz et al. (Somatic Cell and Mol. Genet. 1998. 24: 53-69), Cha et al. (Biotech. and Bioeng. 2000. 67: 555-574), Pryor et al. (Protein Exp. And Purif. 1997. 10: 309-319) and Huston et al. (Int Rev. Immunol. 1993. 10: 195-217).

The teachings of Suteliffe (U. S. Patent No. 5,242798) are set forth above at paragraph 9 but the reference fails to teach that a fusion partner is a His-tag as in claims 67, 71, 75, 76 and GFP as in claims 67-71, and antigen-targeting single chain Fv as in claims 67 and 68 and cleavage site as in claim 77.

Metz et al. teach a vector containing one or two IRES sites and GFP to generate a protein from different IRES sites (see p. 53, abstract; p. 55, Fig1). Cha et al. teach a GFP-fusion protein as a non-invasive quantitative marker to monitor the study protein (i.e. as in claims 67, 71, 75, 76; see p. 555, 2nd col. 1st paragraph). Cha et al. also teach a vector containing a His6-tag and GFP to generate a fusion protein of His-GFP and a cleavage site (i.e. as in claims 67-71, 75-77; see p. 555, abstract). Pryor et al. teach proteins can be isolated by fusing the proteins to a His6-tag (i.e. as in claims 67, 71, 75, 76; see p. 309, abstract). Huston et al. teach fusion proteins to a single chain Fv for immunotargeting of the effector protein such as single-chain Fv toxin fusion proteins (i.e. as in claims 67 and 68; see p. 195, abstract).

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to fuse the claimed polypeptide to GFP or His or Fv for monitoring the expression or location of the protein or purification of the protein. The person of ordinary skill in the art would have been motivated to do so because GFP, His6 and Fv have successfully been used in making a fusion protein for purification,

quantitative and therapeutic purposes. Thus, one of ordinary skill in the art would have expected success in generation of a GFP or His6-tag or Fv fusion protein containing the amino acid sequence of SEQ ID NO:6 or aa 30-72 of SEQ ID NO:6 since fusion proteins of SEQ ID NO:6 have been identified by Suteliffe (U. S. Patent No. 5,242798) containing the last 72-amino acid of the PLP.

11. Claims 61-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stoffel et al. (Hoppe-Seyler's Z. Physiol. Chem. 1982. S. 1117-1131 in view of Metz et al. (Somatic Cell and Mol. Genet. 1998. 24: 53-69), Cha et al. (Biotech. and Bioeng. 2000. 67: 555-574) and Pryor et al. (Protein Exp. And Purif. 1997. 10: 309-319) as applied to claims 61-67, 69-78 above, and further in view of Huston et al. (Int Rev. Immunol. 1993. 10: 195-217).

The teachings of Stoffel et al., Metz et al., Cha et al. and Pryor et al. are set forth in the previous office action and above at paragraph 8 but the references fail to teach that a fusion partner is an antigen-targeting single chain Fv as in claims 67 and 68.

Huston et al. (Int Rev. Immunol. 1993. 10: 195-217) is as set forth above at paragraph 10.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to fuse the claimed polypeptide to GFP or His or Fv for monitoring the expression or location of the protein or purification of the protein. The person of ordinary skill in the art would have been motivated to do so because GFP, His6 and Fv have successfully been used in making a fusion protein for purification,

quantitative and therapeutic purposes. Thus, one of ordinary skill in the art would have expected success in generation of a GFP or His6-tag or Fv fusion protein containing the amino acid sequence of SEQ ID NO:6 or aa 30-72 of SEQ ID NO:6 since fusion proteins of SEQ ID NO:6 have been identified by Suteliffe (U. S. Patent No. 5,242798) containing the last 72-amino acid of the PLP.

Conclusion

12. NO CLAIM IS ALLOWED.

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

AAP50651

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ID   AAP50651 standard; protein; 121 AA.
AC   AAP50651;
DT   25-MAR-2003  (revised)
DT   21-NOV-1991  (first entry)
DE   Sequence encoded by brain specific (Class III ) clone p1B208.
KW   Neurotransmitter; neuromodulator; neuroactive; brain cell proteinoid.
OS   Rattus norvegicus.
PN   AU8430813-A.
PD   24-JAN-1985.
PF   18-JUL-1984;   84AU-00030813.
PR   21-JUL-1983;   83US-00516136.
PR   03-JUN-1987;   87US-00058620.
PA   (SCRI ) SCRIPPS CLINIC & RES FOUND.
PI   Sutcliffe JG;
DR   WPI; 1985-062448/11.
DR   N-PSDB; AAN50475.
PT   New synthetic poly:peptide(s) - useful as neuro-active agents and for
PT   diagnosis of brain cell proteinoid(s).
PS   Disclosure; Fig 7C; 97pp; English.
CC   The peptides of the invention (AAP50641-P50648) can pass from the blood
CC   stream through the blood-brain barrier and into brain cell tissues. They
CC   may be neuroactive, e.g. some cpds. have neurotransmitter-like and
CC   neuromodulating activity. The patent application outlines procedures that
CC   are useful in identifying proteinoids that are translated from brain-
CC   specific mRNA and for preparing synthetic polypeptides whose AA residue
CC   sequences correspond substantially to the AA residue sequences of at
CC   least a portion of those proteinoids. The adult male rat was chosen as a
CC   model. Four brain-specific clones of Class III were described as
CC   exemplary. These clones are designated p1A75, p1B236, p1B208 and p0-40
CC   (see AAN50473-N50475, AAN50520). (Updated on 25-MAR-2003 to correct PA
CC   field.)
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SQ   Sequence 121 AA;

  Query Match             100.0%;  Score 372;  DB 1;  Length 121;
  Best Local Similarity   100.0%;  Pred. No. 9.1e-40;
  Matches   72;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MYGVLPWNAFPGKVCGSNLLSICKTAEFQMTFHLFIAAFVGAAATLVSLLTFMIAATYNF 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         50 MYGVLPWNAFPGKVCGSNLLSICKTAEFQMTFHLFIAAFVGAAATLVSLLTFMIAATYNF 109

Qy         61 AVLKLMGRGTKF 72
              ||||||||||||
Db        110 AVLKLMGRGTKF 121

Q9P2Z7_HUMAN
ID   Q9P2Z7_HUMAN   PRELIMINARY;   PRT;    84 AA.
AC   Q9P2Z7;
DT   01-OCT-2000, integrated into UniProtKB/TrEMBL.
DT   01-OCT-2000, sequence version 1.
DT   07-FEB-2006, entry version 10.
DE   Major myelin proteolipid (Fragment).
GN   Name=PLP;
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae;
OC   Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   NUCLEOTIDE SEQUENCE.
RX   MEDLINE=93278399; PubMed=7684945;
RA   Pham-Dinh D., Boespflug-Tanguy O., Mimault C., Cavagna A., Giraud G.,
RA   Leberre G., Lemarec B., Dautigny A.;
RT   "Pelizaeus-Merzbacher disease: a frameshift deletion/insertion event
RT   in the myelin proteolipid gene.";
RL   Hum. Mol. Genet. 2:465-467(1993).
CC   ---------------------------------------------------------------------
CC   Copyrighted by the UniProt Consortium, see http://www.uniprot.org/terms
CC   Distributed under the Creative Commons Attribution-NoDerivs License
CC   ---------------------------------------------------------------------
DR   EMBL; S62086; AAB26927.2; -; Genomic_DNA.
DR   Ensembl; ENSG00000123560; Homo sapiens.
DR   InterPro; IPR001614; Myelin_PLP.
DR   PANTHER; PTHR11683; Myelin_PLP; 1.
DR   Pfam; PF01275; Myelin_PLP; 1.
DR   SMART; SM00002; PLP; 1.
DR   PROSITE; PS01004; MYELIN_PLP_2; 1.
FT   NON_TER       1      1
SQ   SEQUENCE   84 AA;  8946 MW;  F629EB1144E53CC1 CRC64;

  Query Match             100.0%;  Score 372;  DB 2;  Length 84;
  Best Local Similarity   100.0%;  Pred. No. 1.5e-33;
  Matches   72;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MYGVLPWNAFPGKVCGSNLLSICKTAEFQMTFHLFIAAFVGAAATLVSLLTFMIAATYNF 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         13 MYGVLPWNAFPGKVCGSNLLSICKTAEFQMTFHLFIAAFVGAAATLVSLLTFMIAATYNF 72

Qy         61 AVLKLMGRGTKF 72
              ||||||||||||
Db         73 AVLKLMGRGTKF 84
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14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday and every other Friday from 8:30 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at (571) 272-0841.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/
Chang-Yu Wang, Ph.D.
July 31, 2007

CHRISTINE J. SAOUD
PRIMARY EXAMINER
Christine J. Saoud